

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US91/04078

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC(5):C12Q 1/68;C12P 19/34;G01N 33/48,33/566;C07H 15/12 U.S. CL.: 435/6,91; 436/94,501;536/26,27,28,29																	
II. FIELDS SEARCHED <div style="text-align: center; margin-top: 10px;">Minimum Documentation Searched ⁷</div> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%; padding: 5px;">Classification System</td> <td style="padding: 5px;">Classification Symbols</td> </tr> <tr> <td style="padding: 5px;">U.S. CL.:</td> <td style="padding: 5px;">435/6,91; 436/94,501; 536/26,27, 28, 29; 935/77,78</td> </tr> </table> <div style="text-align: center; margin-top: 10px;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸</div> <p style="margin-top: 10px;">Computer Search: Dialog one search</p>			Classification System	Classification Symbols	U.S. CL.:	435/6,91; 436/94,501; 536/26,27, 28, 29; 935/77,78											
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U.S. CL.:	435/6,91; 436/94,501; 536/26,27, 28, 29; 935/77,78																
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹ <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%; padding: 5px;">Category ⁹</th> <th style="width: 70%; padding: 5px;">Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²</th> <th style="width: 20%; padding: 5px;">Relevant to Claim No. ¹³</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">Belfort et al., eds. "RNA: Catalysis. Splicing. Evolution" published 1989 by Elsevier (Amsterdam). see pages 83-87.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-39</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">Biochemistry. Vol. 26. No. 6. issued 1987. Romaniule et al.. "RNA Binding Site of R17 Coat Protein". pages 1563-1568. see entire paper.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-39</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">Biochemistry. vol. 22. no. 11. issued 1983. Carey et al.. "Sequence Specific Interaction of R17 Coat Protein with its Ribonucleic Acid Binding Site". pages 2601-2610. See page 2603. column 1.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-39</td> </tr> <tr> <td style="text-align: center; vertical-align: top; padding: 5px;">Y</td> <td style="padding: 5px;">Nucleic Acids Research, Vol. 17. No. 2. issued 1989. Joyce et al.. "A Novel Technique for the Rapid Producing of Mutant RNAs". pages 711-722, see entire paper.</td> <td style="text-align: center; vertical-align: top; padding: 5px;">1-39</td> </tr> </tbody> </table>			Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	Y	Belfort et al., eds. "RNA: Catalysis. Splicing. Evolution" published 1989 by Elsevier (Amsterdam). see pages 83-87.	1-39	Y	Biochemistry. Vol. 26. No. 6. issued 1987. Romaniule et al.. "RNA Binding Site of R17 Coat Protein". pages 1563-1568. see entire paper.	1-39	Y	Biochemistry. vol. 22. no. 11. issued 1983. Carey et al.. "Sequence Specific Interaction of R17 Coat Protein with its Ribonucleic Acid Binding Site". pages 2601-2610. See page 2603. column 1.	1-39	Y	Nucleic Acids Research, Vol. 17. No. 2. issued 1989. Joyce et al.. "A Novel Technique for the Rapid Producing of Mutant RNAs". pages 711-722, see entire paper.	1-39
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<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>¹⁰ Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>																	
IV. CERTIFICATION <table style="width: 100%;"> <tr> <td style="width: 50%; vertical-align: top;"> Date of the Actual Completion of the International Search <div style="text-align: center; font-size: 1.2em;">08 October 1991</div> </td> <td style="width: 50%; vertical-align: top;"> Date of Mailing of this International Search Report <div style="text-align: center; font-size: 1.5em;">21 OCT 1991</div> </td> </tr> <tr> <td style="vertical-align: top;"> International Searching Authority <div style="text-align: center;">ISA/US</div> </td> <td style="vertical-align: top;"> Signature of Authorized Officer <div style="text-align: center;"> Stephanie W. Zitomer Ph.D. </div> </td> </tr> </table>			Date of the Actual Completion of the International Search <div style="text-align: center; font-size: 1.2em;">08 October 1991</div>	Date of Mailing of this International Search Report <div style="text-align: center; font-size: 1.5em;">21 OCT 1991</div>	International Searching Authority <div style="text-align: center;">ISA/US</div>	Signature of Authorized Officer <div style="text-align: center;"> Stephanie W. Zitomer Ph.D. </div>											
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FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE¹

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☐ Claim numbers _____, because they relate to subject matter^{1,2} not required to be searched by this Authority, namely:
2. ☐ Claim numbers _____, because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out^{1,2}, specifically:
3. ☐ Claim numbers _____, because they are dependent claims not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. ☒ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING³

This International Searching Authority found multiple inventions in this international application as follows:

- I- Claims 1-23, 30-39 comprise a first product and process of using.
- II- Claims 24-29 comprise a second process.
- III- Claims 40-90 comprise a second product.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:
3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:
4. ☒ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

- ☐ The additional search fees were accompanied by applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
Y	<p>Proceedings National Academy of Science. USA, Vol. 63, issued 1969. Cohen et al.. "Interactions of Hormonal Steroids with Nucleic Acids, i. A specific Requirement for Guanine". pages 458-464, see abstract.</p>	40-90

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 February 2001 (08.02.2001)

PCT

(10) International Publication Number
WO 01/09390 A1

(51) International Patent Classification⁷: C12Q 1/68, C12P
19/34, C07H 21/02, 21/04

(74) Agents: SWANSON, Barry, J. et al.; Swanson &
Bratschun, L.L.C., Suite 330, 1745 Shea Center Drive,
Highlands Ranch, CO 80126 (US).

(21) International Application Number: PCT/US00/02167

(22) International Filing Date: 28 January 2000 (28.01.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/364,902 29 July 1999 (29.07.1999) US

(71) Applicant (for all designated States except US): NEXS-
TAR PHARMACEUTICALS, INC. [US/US]; Suite 200,
2860 Wilderness Place, Boulder, CO 80301 (US).

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ,
BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK,
DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent
(AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent
(AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM,
GA, GN, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

(75) Inventors/Applicants (for US only): HICKE, Brian
[US/US]; 3255 6th Street, Boulder, CO 80304 (US).
WARREN, Stephen [US/US]; 1095 Utica Avenue,
Boulder, CO 80304 (US). PARMA, David [US/US]; 6140
Habitat Drive, Boulder, CO 80301 (US). GOLD, Larry
[US/US]; 1033 5th Street, Boulder, CO 80302 (US).

Published:

— With international search report.

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: TENASCIN-C NUCLEIC ACID LIGANDS

(57) Abstract: Methods are described for the identification and preparation of nucleic acid ligands to tenascin-C. Included in the invention are specific RNA ligands to tenascin-C identified by the SELEX method. Further included in the invention are methods for detecting the presence of a disease condition in a biological tissue in which tenascin-C is expressed.

WO 01/09390 A1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/02167

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; C12P 19/34; C07H 21/02, 21/04

US CL : 435/6, 91.2; 536/23.1, 24.3, 25.4

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/6, 91.2; 536/23.1, 24.3, 25.4

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
WEST, DIALOG ONESEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,475,096 A (GOLD et al.) 12 December 1995, column 5, paragraph 2; column 8, lines 22-48; column 14	1-43
Y	US 5,859,228 A (JANJIC et al.) 12 January 1999, see entire document	15-43
Y	MERLO, A. et al. Biodistribution of ¹¹¹ In-labeled SCN-bz-DTPA-BC-2 Mab Following Loco-regional Injection into Glioblastomas, Int. J. Cancer 1997. Vol. 71. pages 810-816, see entire document	15-43

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Z* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

12 MAY 2000

Date of mailing of the international search report

08 JUN 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

STEPHANIE ZITOMER, PHD

Telephone No. (703) 308-0196

PATENT COOPERATION TREATY

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

To:

SWANSON, Barry, J.
Swanson & Bratschun, L.L.C.
Suite 330
1745 Shea Center Drive
Highlands Ranch, CO 80126
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)

15 janvier 2002 (15.01.02)

Applicant's or agent's file reference

NEX 86/PCT

IMPORTANT NOTIFICATION

International application No.

PCT/US00/02167

International filing date (day/month/year)

28 janvier 2000 (28.01.00)

1. The following indications appeared on record concerning:



the applicant



the inventor



the agent



the common representative

Name and Address

NEXSTAR PHARMACEUTICALS, INC.
Suite 200
2860 Wilderness Place
Boulder, CO 80301
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:



the person



the name



the address



the nationality



the residence

Name and Address

GILEAD SCIENCES, INC.
333 Lakeside Drive
Foster City, CA 94404
United States of America

State of Nationality

US

State of Residence

US

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:



the receiving Office



the International Searching Authority



the International Preliminary Examining Authority



the designated Offices concerned



the elected Offices concerned



other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Philippe Bécamel

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year)

19 July 2001 (19.07.01)

International application No.

PCT/US00/02167

Applicant's or agent's file reference

NEX 86/PCT

International filing date (day/month/year)

28 January 2000 (28.01.00)

Priority date (day/month/year)

29 July 1999 (29.07.99)

Applicant

HICKE, Brian et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

01 February 2001 (01.02.01)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Antonia Muller

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

REC'D 08 MAY 2001

WIPO

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT


(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NEX 86/PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/02167	International filing date (day/month/year) 28 JANUARY 2000	Priority date (day/month/year) 29 JULY 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant NEXSTAR PHARMACEUTICALS, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 4 sheets.
- ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 01 FEBRUARY 2001	Date of completion of this report 17 APRIL 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer STEPHANIE ZITOMER, PHD  Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/02167

I. Basis of the report**1. With regard to the elements of the international application:***☒ the international application as originally filed☒ the description:pages 1-30 , as originally filedpages NONE , filed with the demandpages NONE , filed with the letter of _____☒ the claims:pages 31-37 , as originally filedpages NONE , as amended (together with any statement) under Article 19pages NONE , filed with the demandpages NONE , filed with the letter of _____☒ the drawings:pages 1-8 , as originally filedpages NONE , filed with the demandpages NONE , filed with the letter of _____☒ the sequence listing part of the description:pages NONE , as originally filedpages NONE , filed with the demandpages NONE , filed with the letter of _____**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).☐ the language of publication of the international application (under Rule 48.3(b)).☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**☐ contained in the international application in printed form.☐ filed together with the international application in computer readable form.☐ furnished subsequently to this Authority in written form.☐ furnished subsequently to this Authority in computer readable form.☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.**4. ☒ The amendments have resulted in the cancellation of:**☒ the description, pages NONE☒ the claims, Nos. NONE☒ the drawings, sheets/fig NONE**5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).****

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

**Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/02167

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)

Claims	<u>1-43</u>	YES
Claims	<u>NONE</u>	NO

Inventive Step (IS)

Claims	<u>1-43</u>	YES
Claims	<u>NONE</u>	NO

Industrial Applicability (IA)

Claims	<u>1-43</u>	YES
Claims	<u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1-43 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed invention. The claimed invention encompasses nucleic acid ligands to tenascin-C, complexes comprising a ligand and a marker for *in vivo* diagnostics such as a radionuclide including indium 111, iodine 131 and phosphorous 32 or fluorophore, methods for making the nucleic acid ligand complexes via SELEX and methods using the complexes to detect and treat a disease such as cancer or psoriasis.

Gold et al. (5,475,096) disclose the SELEX method of identifying nucleic acid ligands to a target protein that is recited in instant claims 1-4 and 10-14 and nucleic acid ligands to protein targets as recited in instant claims 1-9 (beginning at column 5, lines 20-34). Gold et al. further disclose the production of nucleic acid antibodies via SELEX (column 30, lines 40-53), use of nucleic acid antibodies for targeting biological structures (column 27, lines 63-67) and therapeutic use for drug delivery (column 8, lines 46-48). The claimed invention differs from Gold et al. wherein the nucleic acid ligand is to tenascin-C and is complexed with a marker for *in vivo* diagnostics.

Janjic and Gold et al. 5,859,228) teach nucleic acid ligands complexed with a therapeutic or diagnostic agent such as an imaging agent including radionuclides such as indium 111, iodine 131 and phosphorous 32 or fluorophore (column 15, lines 17-30) for applications to diseases such as cancer or psoriasis (column 21, lines 5-17). Merlo et al. (Int. J. Cancer 71:810-816, 1997) teach conventional antibodies to tenascin-C and their use as drug delivery vehicles in treating cancer (page 810, abstract). The reference also teaches the presence of tenascin-C as "an integral part of the extracellular tumor architecture" (page 810, column 1, last 12 lines). However, none of the references individually or in combination nor general knowledge in the art would have motivated the skilled practitioner in the art to make nucleic acid ligands specific for tenascin-C and complexes thereof with markers for *in vivo* diagnostics because the Gold et al. disclosure is generic with regard to nucleic acid antibodies and (Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/02167

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12Q 1/68; C12P 19/34; C07H 21/02, 21/04 and US Cl.: 435/6, 91.2; 536/23.1, 24.3, 25.4

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Janjic et al. teach nucleic acid ligands to the unrelated protein, vascular endothelial growth factor. One of ordinary skill in the art would have recognized the utility and industrial applicability of the claimed invention nucleic acid ligands to tenascin-C, complexes thereof and methods of making and using in view of such prior art as Merlo et al..

----- NEW CITATIONS -----
NONE